SUMMARY OF THE ENDOCRINE DISRUPTOR PRIORITY-SETTING WORKSHOP

Prepared for:

U.S. Environmental Protection Agency
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NOTICE

This report was prepared by Eastern Research Group, Inc. (ERG), an EPA contractor, as a general record of discussions during the Endocrine Disruptor Priority-Setting Workshop. As requested by EPA, this report captures the main points and highlights of discussions held during the three-day workshop. The report is not a complete record of all details discussed nor does it embellish, interpret, or enlarge upon matters that were incomplete or unclear.

EXECUTIVE SUMMARY

The 1996 Food Quality Protection Act and the Amendments to the Safe Drinking Water Act required EPA to develop a screening program to determine whether certain substances have endocrine effects similar to those produced by naturally occurring hormones. Such substances are known as endocrine disruptors. Implementation of this program was required by August 1999, and a status report on the program must be presented to Congress by August 2000.

In 1996, EPA formed the Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC). The EDSTAC report of August 1998 discussed the Committee's recommendations for many aspects of the endocrine disruptor screening program, including details on priority setting and recommendations for potentially relevant exposure and effects data sources.

EPA's Endocrine Disruptor Screening Program uses a tiered approach for determining whether a substance may have an effect in humans that is similar to an effect produced by naturally occurring estrogen, androgen, or thyroid hormones. The core elements of the tiered approach include Initial Sorting, Priority Setting, Tier One Screening, and Tier Two Testing.

On June 5 through June 7, 2000, EPA hosted a workshop to discuss the current status of the Endocrine Disruptor Screening Program and to solicit comments on Version 2 of the Endocrine Disruptor Priority Setting Database (EDPSD v.2) from the panel members.

The first day of the workshop provided an overview of the EDSP, including: a discussion of the Agency's overall approach to priority-setting; how pesticide active ingredients are being addressed differently than other chemicals; the current status of standardization and validation activities; and the projected time lines for chemical selection and testing. The second and third days of the workshop were spent discussing specific features of the EDPSD, which is now a functional database. Agency representatives described the system and its exposure and effects compartments, and received comments from both invited participants and, to a limited extent, the public on: the specific hazard and exposure data elements included in the database; the ranking algorithms; and tentative screening priority lists that resulted from various ranking options. At the close of the workshop, next steps were summarized.

The major points raised by the panel members are outlined below.

- Increase transparency throughout the User's Guide, including discussion of why the proposed weights, algorithms, etc. were chosen, EPA's data source hierarchy, methods used to rank data sources, weights associated with data sources, compartments and categories, and EPA's methodology used to select both the ranking technique and the assigned weights.

- Prepare several alternate ranking scenarios. Summarize and discuss the results of each approach on the chemicals selected for the Tier 1 Screening List. Present the results of the multiple ranking scenarios and summarize how these were used.

- Expand the amount of effects data incorporated into EDPSD v.2.

- Calculate chemical ranks in the Combined Exposure- and Effects-Related Information Category using a multiplicative relationship to capture chemicals with a moderate level of risk and a moderate level of exposure.

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1.0 INTRODUCTION AND REPORT ORGANIZATION

The 1996 Food Quality Protection Act and the Amendments to the Safe Drinking Water Act require EPA to develop a screening program to determine whether certain substances have endocrine effects similar to those produced by naturally occurring hormones. Such substances are known as endocrine disruptors. Implementation of this program was required by August 1999, and a status report on the program must be presented to Congress by August 2000.

In 1996, EPA formed the Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC). The EDSTAC report of August 1998 discussed the Committee's recommendations for many aspects of the endocrine disruptor screening program, including details on priority setting and recommendations for potentially relevant exposure and effects data sources.

EPA's Endocrine Disruptor Screening Program (EDSP) uses a tiered approach for determining whether a substance may have an effect in humans that is similar to an effect produced by naturally occurring estrogen, androgen, or thyroid hormones. The core elements of the tiered approach include Initial Sorting, Priority Setting, Tier One Screening, and Tier Two Testing.

The data collected through the screening program will help identify and characterize hazard (potential to cause harm). When all of the hazard data are integrated and interpreted, a hazard assessment will be performed. EPA will then perform an exposure assessment by looking at how many humans or how much wildlifeis likely to be exposed to the chemical. The final step in the process is the risk assessment, where EPA will integrate the information about how potentially harmful a chemical is with the likelihood that someone or something will be exposed to it. Based on the risk assessment, EPA will determine how best to manage the chemical.

Version 2 of the Endocrine Disruptor Priority-Setting Database (EDPSD v.2) supports the priority setting phase of the Endocrine Disruptor Screening Program. This tool is being developed by a workgroup of Office of Prevention, Pesticides, and Toxic Substances (OPPTS) scientists to use in prioritizing chemicals for Tier 1 Screening in the EDSP. Version 1 of EDPSD was developed to support the work of EDSTAC.

The Endocrine Disruptor Priority-Setting Workshop was held on June 5 through June 7, 2000. The notice for the meeting was published in the Federal Register on May 19, 2000. EPA staff, invited participants, and the public attended the meeting. Day 1 of the meeting included an overview of the entire EDPSD was presented on Day 1 of the meeting. This overview included: a discussion of the Agency's overall approach to priority-setting; how pesticide active ingredients are being addressed differently than other chemicals; the current status of standardization and validation activities; and the projected time lines for chemical selection and testing. The second and third days of the workshop were spent discussing specific features of the EDPSD. Agency representatives described the systems's components and functionality, as well as its exposure and effects compartments. Comments from panel discussions with invited participants and, to a limited extent, public inquiries were received on: the specific hazard and exposure data elements

included in the database; the ranking algorithms; and tentative screening priority lists that resulted from various ranking options. At the close of the workshop, next steps were summarized.

This report summarizes the information presented during the workshop, as well as public and panelist comments. The report sections are organized as follows:

- Section 2: Summarizes opening remarks;
- Section 3: Discusses the comments to the overview of the Endocrine Disruptor Screening Program;
- Section 4: Summarizes the Endocrine Disruptor Screening Program Validation;
- Section 5: Discusses prioritization of pesticide active ingredients;
- Section 6: Summarizes the public comments made on Day 1 of the Workshop;
- Section 7: Discusses the Endocrine Disruptor Priority Setting Database including:
  - -- An overview of the current status of EDPSD v.2,
  - -- The completeness and quality of the data sources used in the exposure compartments,
  - -- The ranking algorithms used in exposure compartments,
  - -- The completeness and quality of the data sources used in the human effects compartments,
  - -- The ranking algorithms used in the human effects compartments,
  - -- The completeness and quality of the data sources and the ranking algorithms used in the ecological effects compartments,
  - -- The definition of and ranking procedures for the combined compartments,
  - -- The database default weights,
  - -- EPA's policy decision to focus on the intersect of High Production Volume (HPV) chemicals and pesticide other ingredient compounds; and
  - -- General questions related to EDPSD v.2.
- Section 8: Summarizes public comments from Days 2 and 3 of the Workshop; and
- Section 9: Discusses the next steps.

2.0 OPENING REMARKS

Dr. Steve Galson, Director, US EPA Office of Science Coordination and Policy (OSCP)

After welcoming and thanking the workshop attendees, Dr. Galson described the types of input EPA hoped to receive during the workshop, including comments on the basic logic of the priority-setting approach, the data sources selected, and the compartment weightings. Dr. Galson reiterated EPA's commitment to transparency, and indicated EPA's intention for the program to be flexible, to incorporate new information as it becomes available, and to reflect changing judgements about data parameters. EPA would like input on the current level of transparency and any other participant concerns.

Dr. Galson also indicated that the OSCP website would post a meeting summary within 45 days, and that written comments were to be submitted within 30 days of the summary report posting.

Dr. Galson recognized the importance and efforts of the workshop participants and the EPA staff supporting the Endocrine Disruptor Screening Program.

Agenda Review
Tim Mealey, MERIDIAN Instititute

Mr. Mealey reviewed the agenda and logistics of the workshop.

3.0 OVERVIEW OF THE ENDOCRINE DISRUPTOR SCREENING PROGRAM

Jim Kariya, US EPA Office of Science Coordination and Policy

Mr. Kariya presented an overview of the Endocrine Disruptor Screening Program (EDSP). This presentation can be viewed at *http://www.epa.gov/scipoly/oscpendo/prioritysetting/jkpsdboverview.ppt*, and is summarized below:

- The Food Quality Protection Act and amendments to the Safe Drinking Water Act provide the regulatory requirements for EDSP.

- The EDSTAC process and the recommendations of the committee resulted in a final EDSTAC report. This report published in 1998, can be found at *http://www.epa.gov/scipoly/oscpendo/history/finalrpt.htm*

- EPA published an EDSP proposed policy statement in the Federal Register on December 28, 1998. This policy statement can be found at *http://www.epa.gov/scipoly/oscpendo/fr122898_1.pdf*

- Since the EDSTAC review, EPA has implemented the following:

  -- The High-Throughput Pre-Screening (HTPS) demonstration project,
  -- Development of the priority-setting database,
  -- Investigation of quantitative structure activity relationships (QSARs), and
  -- Standardization and validation activities.

- Upcoming Endocrine Disruptor Screening Program activities include:

  -- Preparation of a Report to Congress in August 2000 describing findings to date, recommendations for further testing, and recommendations for further action,
  -- Convening of an Advisory Committee on Standardization and Validation, and
  -- Development of a Procedural Rule that will specify the list of chemicals to be tested, the test battery, and the review process.

- The time line for the endocrine disruptor screening program is as follows:

  -- Priority-setting is anticipated to be completed by the end of 2001,
  -- Tier 1 Validation is anticipated to be completed by the beginning of 2003,

-- Tier 2 Validation is anticipated to be completed by the mid-2005, and
-- Phase I screening is expected to be started in 2003 and completed by the end of 2005.

4.0 ENDOCRINE DISRUPTOR SCREENING PROGRAM VALIDATION

Gary Timm, US EPA Office of Science Coordination and Policy

Mr. Timm presented an update on the Endocrine Disruptor Screening Program Validation activities. This presentation can be viewed at *http://www.epa.gov/scipoly/oscpendo/stdvalgt.ppt*, and is summarized below:

- EPA proposed using a two-tier process for endocrine disruptor screening and testing, which includes:

  -- Tier 1 Screening to identify substances for further testing and
  -- Tier 2 Testing to identify adverse effects and establish dose-response relationships for Hazard Assessment.

- The criteria for Tier 1 screens includes:

  -- How the data will be used,
  -- The modes of action that will be tested,
  -- The proposed screening battery, and
  -- Alternate assays.

- The types of information EPA anticipates collecting from the Tier 2 tests and the proposed Tier 2 testing battery can be viewed on the website.

- EPA plans to replace the existing Endocrine Disruptor Screening and Testing Validation and Standardization task force with a Federal Advisory Committee Act (FACA) committee. The committee is expected to convene by September 2000.

- Coordination among EPA, the Interagency Coordinating Committee for Validation of Alternate Test Methods (ICCVAM), and VS FACA is necessary for the validation process, statutory requirements for validation, stakeholder involvement in the validation process, validation test methods, and the validation time line.

- Sample screening batteries include how assay choice impacts the actual assays that need to be performed. EPA is performing ongoing work on the assays.

- The status of the research and development, demonstration, standardization, and validation of the Tier 1 and Tier 2 assays as well as the expected completion dates are posted on the website.

- Tier 1 and Tier 2 Validation program projected completion dates were presented.

- The Endocrine Disruptor Screening Program time line was reviewed.

Workshop attendee comments on Mr. Timm's presentation and EPA's responses to those comments during the workshop are summarized below:

Non-Animal Testing Methods

- One participant questioned whether the estrogen receptor and androgen receptor binding assays are always coupled with cell cultures, and was concerned that EPA was rejecting protein binding assays. EPA responded that they will review cell-free as well as other assays.

- One participant inquired as to the level of resources being spent by EPA's Office of Research and Development on researching non-animal test methods. EPA responded that they do not have that information at this time, but it is not likely a large amount. The National Institute of Environmental Health Science (NIEHS) has a specific mandate to focus on non-animal testing methods.

Validation

- A participant was concerned that EPA was considering performing "paper" validation of receptor binding assays since HTPS showed problems with variability and sensitivity. The participant suggested that EPA needs to research the cause of these issues. EPA indicated that laboratory development of androgen receptor cell-lines is underway, and that EPA does not want to limit laboratories to a specific cell-line or approach. EPA's review will be based on what has been successful and demonstrated in the literature. EPA is not aware of any successful and ready-to-use HTPS demonstration data, and is instead focusing on several promising QSAR approaches.

- A participant inquired as to why some assays will be reviewed by ICCVAM and some only by EPA. EPA responded that because of limited resources and time, and since ICCVAM wanted to focus on non-animal testing methods, proposed animal testing methods will be reviewed only by EPA. ICCVAM will also be part of the FACA committee, and will be consulted during protocol development, pre-validation, and validation. In addition, EPA will be developing a background review document that will be almost identical to the ICCVAM background review document.

- Another participant indicated that in the March meeting of the Advisory Panel for Alternative Methods for the National Toxicology Program

(NTP), ICCVAM review of both in-vivo and in-vitro methods was proposed and adopted. The participant was concerned that only in vivo test methods would be evaluated for the endocrine disruptor screening program. The participant requested that EPA review all potential test methods. The participant also had concerns with EPA's validation process, and indicated that it conflicted with the NTP advisory panel decision. EPA indicated that ICCVAM met in April and did not accept the advice of the NTP advisory panel. EPA further indicated that this current validation process is the most rigorous validation process EPA has implemented, that it is an interlaboratory process, and that it will undergo review by the Science Advisory Panel.

QSARs

- One attendee was concerned that much of the SAR work is based on in-vitro studies, and since reliable receptor binding data is critical, the participant questioned whether EPA had enough data on which to base QSARs. EPA responded that the Food and Drug Administration (FDA) has completed data collection for 220 compounds. Their goal is to expand the data set to include 500 compounds. EPA anticipates that the baseline data will be robust.

- Another attendee suggested that the validation and testing process EPA intends to implement is unstructured, and may result in the generation of conflicting data since many different cell-lines will be used. The participant suggested that EPA propose a more definitive approach. EPA responded that they will focus on the successful assays (approximately one dozen).

Chemicals Included in the Endocrine Disruptor Screening Program

- One commenter requested clarification on the chemicals included in the endocrine disruptor screening program. EPA indicated that pesticide active ingredients are being prioritized separately. Of the 87,000 chemicals identified by EDSTAC, EPA chose the approximately 600 chemicals that are on both the High Production Volume (HPV) Challenge Program list and the pesticide other ingredients (formerly " pesticide inerts") list, because exposure to these chemicals is likely higher than with others. Following completion of this phase of the program, EPA intends to consider the full universe of chemicals.

- An attendee was concerned that the HPV list may include some chemicals that are no longer in production. The attendee inquired as to whether EPA would update the list prior to Phase I. EPA indicated that this issue would be addressed prior to Phase I.

General Comments

- One attendee was concerned that EPA omitted mentioning the Scientific Advisory Board/Scientific Advisory Panel (SAB/SAP) joint advisory committee review of EPA's proposed endocrine disruptor screening program. EPA responded that the omission was an oversight, and that this review was a significant part of the program.

5.0 PESTICIDE ACTIVE INGREDIENTS PRIORITY-SETTING FOR THE ENDOCRINE DISRUPTOR SCREENING PROGRAM

Penny Fenner-Crisp, US EPA Office of Pesticide Programs (OPP)

Dr. Fenner-Crisp presented an update on the Endocrine Disruptor Screening Program activities related to pesticide active ingredients. This presentation can be viewed at *http://www.epa.gov/scipoly/oscpendo/edpsdworkshoppfc.ppt*, and is summarized below:

- Under the Food Quality Protection Act (FQPA), EPA must screen pesticides (actives and others) for estrogenic effects that may affect human health, and may include other effects.

- The proposed implementation strategy for the 950 U.S. registered active ingredients, 450 of which have food/feed uses, and the 2,500 "other" ingredients (previously referred to as "inerts") includes:

  -- Exempting, sorting, and prioritizing other ingredients using EDPSD v.2,
  -- Revising 40 Code of Federal Regulations (CFR) 158 to include endocrine disruptor screening,
  -- Running a pilot program for between 25 and 50 active ingredients, and
  -- The potential issuing of orders for groups of substances.

- The overlap of the pesticide other ingredients and pesticide active ingredient review process with the overall Endocrine Disruptor Screening Program process was discussed. Already-registered actives are anticipated to fall into Category 3 (i.e., adequate screening data are currently available; however, additional toxicity data will be needed to determine estrogen, androgen, and thyroid disruption potential) or 4 (data are adequate for hazard assessment).

- CFR Part 158 has toxicology and ecological effects testing requirements.

- The proposed Tier 1 Screening and Tier 2 Testing Batteries, and a list of alternate Tier 2 battery tests can be viewed on the website.

- EPA has developed a proposed implementation strategy for the already registered pesticide active ingredients, other ingredients, and not-yet-registered pesticide active ingredients.

Workshop attendee comments on Dr. Fenner-Crisp's presentation and EPA's responses to those comments during the workshop are summarized below:

- One attendee questioned how the confidential status of pesticide other ingredients will impact the review process. EPA agreed that this needs to be addressed.

- Another attendee was interested in EPA's approach for prioritizing pesticide other ingredients produced in quantities of less than 10,000 pound annual production volume. EPA indicated that although these chemicals will not be part of Phase I, they will be covered in later phases of the program.

- An attendee requested clarification of the overlap of EPA's pilot program evaluation of existing data with the pesticide tolerance reassessment schedule. EPA responded that these two programs are indirectly related. Pilot program chemicals may already be in the middle of the tolerance reassessment process, already have their reassessment completed, or have not yet begun their reassessment.

- An attendee inquired as to whether manufacturers could substitute data from other assays for the multi-generational studies. EPA responded that it could be done.

- If test method validation is currently ongoing, one attendee was concerned about the sources for adequate pesticide active ingredient data. EPA indicated that the existing data will come from pre-existing guidelines application data. EPA will review on a case-by-case basis whether the previously generated data are adequate.

- An attendee requested more information on the overlap of endocrine disruptor testing with the HPV Challenge Program. EPA indicated that the endocrine disruptor tests are not a criteria for the HPV program. EPA has had some preliminary discussions with industry regarding a combined approach to these two efforts. Another attendee recommended that EPA not delay the HPV program because it is well underway and the endocrine disruptor tests will not be validated until after the HPV program is completed. The commenter also recommended that EPA incorporate HPV data into the priority-setting database. EPA indicated that it intended to incorporate HPV data into EDPSD v.2.

6.0 PUBLIC COMMENTS ON DAY 1 OF THE WORKSHOP

Public comments received on Day 1 of the Workshop are summarized below:

Chemicals Included in the Endocrine Disruptor Screening Program

- One commenter recommended that EPA include pharmaceuticals and consumer products in the priority-setting process. EPA indicated data for some cosmetic chemicals are in EDPSD v.2, but that only those chemicals that overlap with HPV/pesticide other ingredients would be considered during this phase. EPA is also somewhat limited by statutory authority since pharmaceuticals are regulated by FDA. EPA is discussing this topic with FDA.

Testing Battery

- The Federal Register describes Tier 2 testing as a battery of tests to identify chemicals that cause effects in humans similar to effects from naturally occurring hormones, and to identify, characterize, and quantify these effects for the estrogen, androgen, and thyroid vectors. The commenter does not believe EPA will be able to meet these goals. EPA indicated some of the tests are atypical and the results can be very well attributed, but that some of the test results will be more general. EPA stressed the importance of the Tier 1 results in facilitating this analysis.

Use of Endocrine Disruptor Screening Program Data

- One attendee questioned how the information generated by the EDPSD v.2 will be used in the risk assessment and regulatory process. EPA indicated a number of mandates can be used to regulate chemicals, and that the appropriate one would be chosen. A full risk and exposure assessment and regulatory process consistent with these mandates would be carried out. Overall, EPA indicated that it was not possible at this time to predict the regulatory outcome of the program.

- A commenter suggested EPA give thought to how the results of endocrine disruptor screening and testing can be applied to assessing hazards and environmental impacts. EPA indicated that a workshop on the exposure issues will take place in the fall or early next year, but that additional research will be required to address how to apply the hazard assessment test information to a risk assessment.

- Another commenter recommended that EPA develop a guideline for risk assessment of endocrine disruptors. EPA indicated this task will be completed in a later phase of the program.

HTPS and Validation

- Report on Japanese HTPS Research: Dr. Jun Kanno reported that Japan has developed an HTPS approach to detect estrogenic substances using a stably transfected HeLa cell line for ER∝ with a luciferase reporter. One hundred fifteen chemicals have been studied. The samples of the chemicals to be studied were dissolved in DMSO from which seven test concentrations were prepared ranging from one picomolar to one micromolar. Runs were made with and without the S-9 protein fraction (that is with and without metabolism). The ER data is available and will be provided to EPA, but the AR system needs additional refinement.

  Dr. Kanno also reported that several Japanese researchers are developing QSAR systems. Dr. Itai of the Institute of Medical Molecular design has developed a docking model for ER. This type of model predicts binding by fitting all conformations to the pocket in the receptor. A second model mentioned by Dr. Kanno is being worked on by NIHS. This is the Surface Plasmon Resonance model that predicts conformational change of the ER∝ induced by a ligand. It presumably could distinguish agonists from antagonists.

- HTPS validation, including chemical specificity, interlaboratory validation requirements, and the impact of the expense of HTPS equipment was discussed. The attendee also discussed the use of transferrable technologies, implications of the use of patented cell lines, and whether these data could be incorporated into the Endocrine Disruptor Screening Program Phase I.

- A commenter raised concerns that QSARs and HTPS methods focus on ligand receptor binding only, and do not capture other types of agonist and antagonistic activities.

- Another commenter requested information on whether EPA was pursuing any research activities similar to what is being done in Japan. EPA indicated that assays are being developed for the bench, but none using robotics.

- Another commenter was interested in determining EPA's next steps for HTPS. EPA indicated that no HTPS activities are planned between now and December. However, EPA will coordinate with the contacts working on promising methods in Japan.

General Comments

- One commenter was concerned that releasing the draft priority-setting list, may lead companies to cease manufacturing certain chemicals. EPA indicated priority-setting is only the first step in a lengthy review process. EPA will not keep the list private; it is mandated to release the information to the public. EPA will clearly communicate the limitations of the screening and testing assays.

- Since several EPA initiatives contain similar elements (i.e., HPV Challenge Program, Children's Health Testing, and Endocrine Disruptor Screening), one commenter urged EPA to consolidate efforts.

- Another commenter raised the issue of the NTP Advisory Panel recommendation that both in-vivo and in-vitro assays be validated by ICCVAM. EPA reiterated that the ICCVAM discussed the advisory panel recommendations and did not accept them.

- One commenter suggested that EPA mine existing databases for health effects data. EPA responded that they would incorporate available data as possible, and also plan to incorporate QSARs and results of in-vivo testing.

7.0 THE ENDOCRINE DISRUPTOR PRIORITY SETTING DATABASE

7.1 Background Information on the Endocrine Disruptor Screening Program Mr. James Darr, US EPA, Office of Pollution Prevention and Toxics, Exposure Assessment Branch

Mr. Darr gave a brief overview of the Endocrine Disruptor Screening Program and EDPSD v.2. His presentation can be viewed at *http://www.epa.gov/scipoly/oscpendo/prioritysetting/presentationsonthedatabase2.ppt*. The key points from his presentation are summarized below.

- The four categories which comprise EDPSD v.2 are:

  -- Specially Targeted Priorities (which contains the Mixtures, Nominations, and Naturally Occurring Non-Steroidal Estrogens (NONEs) compartments),
  -- Exposure-Related Information,
  -- Effects-Related Information, and
  -- Combined Exposure- and Effects-Related Information.

- EPA's current focus is on the intersection of HPV chemicals and pesticide other ingredients (HPV/pesticide other ingredients). Relevant collections of data were screened for the Exposure Category and data for all chemicals (including non-HPV/ pesticide other ingredients) were incorporated into EDPSD v.2. Data for HPV/Pesticide other ingredients only were reviewed and incorporated into the Effects Category.

- The main features of the compartment-based priority setting approach are as follows:

  -- Chemicals are selected independently from each compartment,
  -- The weight of each compartment is the fraction of the total number of chemicals selected from all compartments that will come from that compartment. For example, if a compartment has a 20% weight and 100 chemicals are selected overall, 20 chemicals will be from that compartment,
  -- Data source ranking occurs within a compartment, and
  -- The Tier 1 Screening List is **not** rank ordered.

After Mr. Darr's presentation, Grace Kitzmiller of Eastern Research Group (ERG) demonstrated the functionality of EDPSD v.2. Her presentation can be viewed at *http://www.epa.gov/scipoly/oscpendo/prioritysetting/endodemo.ppt*. Her presentation is outlined below.

- EDPSD v.2 software, the associated User's Guide, and the Quick-Start Tutorial can be downloaded from *http://www/erg.web.com/endocrine*.

- EDPSD v.2 consists of four categories, 27 compartments and 50 data sources. It contains information for approximately 143,000 chemicals. Data sources compose compartments and compartments compose categories.

- The primary functions of EDPSD v.2 include:

  -- Generating the Tier 1 Screening List Report,
  -- Viewing EDPSD v.2 data,
  -- Viewing data source and compartment ranking algorithms, and
  -- Performing "What-If"" analyses.

Each of these functions was described in detail during the presentation. The commenters' questions and comments on the presentation, as well as EPA's responses, are summarized below.

Tier 1 Screening List Report

- A panel member asked about the order in which EDPSD v.2 accesses a compartment when generating a Tier 1 Screening List Report. EPA indicated that the number of chemicals selected from each compartment is predetermined by the associated weight; therefore, the order in which the compartments are accessed is not relevant.

- A panel member asked for clarification concerning the number of chemicals processed and the number of chemicals selected. EPA stated that the number of chemicals processed is the actual number of chemicals that EDPSD v.2 accessed (including duplicate chemicals from different compartments) to generate the Tier 1 Screening List. The number of chemicals selected for the Tier 1 Screening List is typically slightly higher than the target number of chemicals entered by the user. EPA indicated that they will clarify the Tier 1 Screening List Report section in future versions of the EDPSD v.2 User's Guide.

EDPSD v.2 Category, Compartment, and Data Source Viewing

- One panel member stated that he experienced problems when trying to view chemical data. He indicated that the Chemical Abstract Service (CAS) number is necessary to determine whether or not data exist for a particular chemical. He stated that in many cases the chemical name he entered did not access data for the chemical he was interested in because of the use of synonyms in EDPSD v.2. He recommended only using the CAS number search functionality when viewing chemical data.

- A panel member was concerned about the lack of effects data in EDPSD v.2. EPA indicated that the Reproductive/Developmental Toxicity Compartment contains the most chemicals and that effects data are scarce for the other compartments.

Compartment Weights

- A panel member asked for clarification concerning relative weights for each compartment. EPA indicated thata compartment's relative weight is a percentage that each compartment represents of the sum of the total weights. The user can change the weights of each compartment independently of one another. For example, if the compartment weights sum to 110%, EDPSD v.2 adjusts the individual compartment relative weights such that the sum of the relative weights equals 100 percent.

7.2 Overview of the Current Status of the Endocrine Disruptor Priority-Setting Database (EDPSD v.2)

Welcome and Brief Overview
Cathy Fehrenbacher, US EPA, Office of Pollution Prevention and Toxics, Chief Exposure Assessment Branch (OPPT/EAB)

Ms. Fehrenbacher welcomed the attendees and provided a brief overview of the current status of EDPSD v.2. She indicated that several data sources have not yet been incorporated, and that a draft priority list of chemicals has not yet been developed.

Current Status and Future Plans for EDPSD v.2
Patrick Kennedy, US EPA, Office of Pollution Prevention and Toxics, Exposure Assessment Branch (OPPT/EAB)

Mr. Kennedy summarized the current status and the future plans for EDPSD v.2. This presentation can be viewed at *http://www.epa.gov/scipoly/oscpendo/prioritysetting/presentationsonthedatabase2.ppt.* His presentation is summarized below.

- EPA developed the draft database using the EDSTAC compartment-based approach, which includes a database of four information categories.

- EPA's current focus is on the intersection of HPV chemicals and pesticide other ingredients (referred to as the HPV/pesticide other ingredients). Approximately 600 chemicals are part of both the HPV and pesticide other ingredients lists.

- The pesticide active ingredients (PAI) are being handled separately, and will be prioritized outside of the EDPSD.

- The exposure compartments contain data on an extensive list of chemicals, including pesticides, metals, volatile organic compounds, HPV chemicals, and pesticide other ingredients. Exposure data sources were only considered if they had data related to the HPV/Pesticide other ingredients, but all chemicals from the selected sources were included in the database.

- The effect compartments contain data only for the HPV/Pesticide other ingredients chemicals, a result of a policy decision based on a number of factors including the level of resources required to extract effects data.

- EPA developed a draft approach to selecting Phase I priority chemicals (the default scenario).

- The current weights associated with each of the four categories is as follows:

Combined Exposure and Effects-Related Information	50%
Exposure-Related Information	20%
Effects-Related Information	25%
Specially Targeted Priorities	5%

- EPA hopes to receive comments on the draft scenario during this workshop.

- The following process is expected to be used to select chemicals for Tier 1 Screening:

  -- Select the draft list of priority chemicals,
  -- Perform internal EPA review of the list for sorting purposes,
  -- Develop the list of priority chemicals, and
  -- Request public comment on the resulting Tier 1 Screening List.

- Future plans for the program include:

  -- Revising the database to address Workshop comments,
  -- Incorporating additional data sources into the Ecological Biological Monitoring Data Compartment and the effects compartments,
  -- Adding QSARs, and
  -- Conducting an external peer-review of the database prior to its use in selecting chemicals for Phase I.

After the presentation, Mr. Kennedy reviewed the list of questions sent to the invited guests and asked for feedback on the topics covered in his presentation. No comments relevant to this topic were provided.

7.3 Completeness and Quality of Data Sources Used in the Exposure Compartments

Patrick Kennedy, US EPA, Office of Pollution Prevention and Toxics, Exposure Assessment Branch (OPPT/EAB)

Mr. Kennedy presented background information on the data sources used in the exposure compartments and posed several questions to the panel. His presentation can be reviewed at *http://www.epa.gov/scipoly/oscpendo/prioritysetting/presentationsonthedatabase2.ppt*. These questions were also posed in the invitation letter (found at *http://www.epa.gov/scipoly/oscpendo/prioritysetting*) and are presented below:

- Are the exposure compartment data sources complete and adequate?
- Are any important data sources missing?
- Are the data sources of sufficient quality?
- Is the documentation for the data sources adequate?

The panel's comments and EPA's responses are summarized below.

Incorporation of Additional Data Sources

- Several panel members expressed concern that breast milk data were not included in EDPSD v.2. It was suggested that European studies be evaluated for incorporation into EDPSD v.2. In particular the Swedish Breast Milk study was recommended for evaluation. EPA indicated that in most cases broad scans for chemicals were not performed on breast milk. In addition, breast milk typically has not been analyzed for many of the HPV/Pesticide other ingredients chemicals; therefore, they did not expect to find additional data for these chemicals.

- Several panel members suggested using regional, state, and local data. EPA suggested that users could incorporate these data using the import pre-ranked data functionality of EDPSD v.2 and perform "What-If" analyses on their own. The members expressed concern over whether these data would be incorporated into EDPSD v.2 for final priority setting. EPA indicated that they may solicit exposure data from the states and regions through other forums.

- Table 8 of the recent United States Geological Survey (USGS) 1998 Report presented the number of sites where water quality criteria were exceeded. It was suggested that these data be used in ranking because it would be reasonable to expect chemicals with more exceedances would have a higher priority.

- One panel member indicated that EPA should use national data sets (sampling throughout the nation) rather than regional data sets (localized

sampling). The panel member also thought that a higher weight should be given to national data sets when compared to the weight given to the regional data sets.

- Some panel members suggested that both pharmaceuticals and dietary supplements should be added to the list of chemicals included in EDPSD v.2. EPA indicated at this time both of these chemical groups are excluded.

- It was also suggested that EPA maintain a list of all data sources evaluated under Phase I and revisit the list during follow-up phases.

Other Comments

- Panel members were concerned that diethylstilbestrol (DES) was not included in EDPSD v.2. EPA explained that based on their limited data source search, DES was not found in the sources they selected for incorporation into EDPSD v.2. The exclusion of exposure data on DES was not intentional. The panel members again expressed their concern and recommend that EPA perform a thorough review of the available data sources.

- Panel members expressed concerns about the summary data used in the Human Biological Monitoring Data Compartment. One panel member suggested that data quality is compromised when summary data are used, since information related to how the population was sampled, the statistics within the study, or how the data were collected is not available.

- One panel member congratulated EPA on their efforts and indicated that EDPSD v.2 was a good system that could be used by many people for many purposes.

- Panel members discussed whether Threshold Limit Values (TLVs), Permissible Exposure Limits (PELs), and Recommended Exposure Limits (RELs) were good assessments of occupational exposure. One panel member stated that these risk-based measurements are often developed using irritation rather than toxic endpoints and should not be used to measure occupational exposure. Another panel member indicated that TLVs, PELs, and RELs were the best data sources for this compartment, and are a direct reflection of workplace exposure. A different panel member indicated that the National Occupational Exposure Survey (NOES) data source was out of date and should not be used in this compartment. EPA indicated that these data sets were the best available to assess occupational exposure.

7.4 Ranking Algorithms Used in Exposure Compartments

Conrad Flessner, US EPA, Office of Pollution Prevention and Toxics, Exposure Assessment Branch (OPPT/EAB)

Mr. Flessner gave a brief presentation on the ranking algorithms used in the exposure compartments. He presented examples of different algorithm types (weighted and advanced). His presentation can be viewed at *http://www.epa.gov/scipoly/oscpendo/prioritysetting/presentationsonthedatabase2.ppt*. Mr Flessner then posed the following questions to the panel members:

- Do the algorithms make sense?
- How can EPA improve or replace these algorithms?

The panel members had numerous comments on the ranking algorithms used in the exposure compartments. These comments ranged from changing the ranking algorithm type to modifying the User's Guide to increase transparency.

General Ranking Algorithm Comments

- Some panel members recommended that EPA use concentration values only to rank chemicals.

- Panel members discussed the ranking methodologies associated with the Occupational Exposure Chemicals Compartment. One panel member suggested that the National Institute for Occupational Safety and Health (NIOSH) RELs not be ranked from highest REL to lowest REL, but that the highest priority should be placed on the compound with the lowest REL. Panel members also noted that an effort was made in the late 1980s-early 1990s to update the PELs. Although this update was remanded by the courts for what the panel member indicated were non-technical reasons, it was suggested that EPA incorporate the updated list of PELs into EDPSD v.2 for ranking.

- One panel member suggested that EPA normalize the tissue data in the Ecological Biological Monitoring Compartment using the percent lipid found in each type of tissue. The compartment could then be ranked using the normalized concentrations rather than the number of detects.

- One panel member suggested using a combination of the maximum and median concentrations rather than the median concentration only for ranking purposes.

Documentation and Transparency Issues

- The persistence and bioconcentration factor discussion in the User's Guide is confusing and the references seem to be out of order.

- In general, panel members indicated that the documentation was adequate, but requested EPA further explain the following:

  -- How each data source was used to rank each compartment,
  -- How each data source was ranked, and
  -- Why compartments were ranked using the selected methods.

  Some panel members indicated that discussion of additional ranking methods considered but not selected would be useful, and believed this information would help EPA defend the priority list (when developed).

- One panel member indicated that they found the Human Biological Monitoring Data Compartment write-up unclear and suggested EPA revise that section of the User's Guide.

- A panel member recommended that EPA be more consistent in the User's Guide (i.e., the National Water Quality Assessment Program (NAWQA) /National Stream Quality Accounting Network (NASQAN) sections). Another panel member indicated that these sections might be more readily understood if the equations used in ranking were presented.

- A panel member suggested that incorporation of a data quality hierarchy table for both data sources and compartments would assist in explaining the ranking algorithms.

- It was recommended that EPA develop a report that presents the differences between "What-If" scenarios developed by users and the EPA default scenario. In addition to creating the report, panel members suggested developing a new section of the User's Guide that describes the default scenario.

"What-If" Scenarios

- Many of the panel members recommended that EPA run several "What-If" scenarios, analyze the results of the different scenarios, and describe the results of the analysis. The scenarios proposed by the panel members included:

  -- Create a "What-If" scenario where the weight of the Combined Exposure- and Effects-Related Information Category is set equal to zero. Create a second scenario where all of the categories except

for the Combined Exposure-and Effects-Related Information Category are set equal to zero. Compare the Tier 1 Screening Lists generated by EDPSD v.2 for each of the scenarios.

-- Create a "What-If" scenario where the Ecotoxicity Compartment is set equal to zero and compare the results of this analysis to the default scenario.

- The panel members requested that EPA prepare two of these "What-If" scenarios for discussion on Day 3 of the workshop. [Note: this request was fulfilled by overnight.] The three scenarios that were run and statistical information presented to the group can be viewed at *http://www.epa.gov/scipoly/oscpendo/prioritysetting/whatifscenarios.htm*. Panel members were interested in assessing the differences between the "What-If" Tier 1 Screening List Report and the default scenario, including the chemicals unique to each scenario, the chemicals included on each list, and the overlap of chemicals on each list.

- Based on the outcome of discussing these new "What-If" scenarios, several of the panel members suggested that EPA develop multiple default scenarios for use in developing the Tier 1 Screening List for Phase 1.

7.5 Completeness and Quality of Data Sources Used in the Human Effects Compartments

James Kwiat, US EPA, Office of Pollution Prevention and Toxics, Risk Assessment Division (OPPT/RAD)

Mr. Kwiat gave an introductory presentation on the completeness and quality of data sources used in the human effects compartment. His presentation can be viewed at *http://www.epa.gov/scipoly/oscpendo/prioritysetting/presentationsonthedatabase2.ppt*. His presentation focused on the following questions:

- Are the effects data sources adequate?
- Is the documentation complete?
- Can adequate data relationship judgements be made using summary data?
- Is the compartment definition clear? Should information be added? Combined? Or split into separate compartments?

The panel members' questions and comments are presented below.

Additional Data Sources

- A panel member recommended that EPA incorporate neurotoxic and neuro-behavioral effects data into EDPSD v.2. EPA indicated these types of effects data were included where appropriate (if the effects were

associated with a reproductive or developmental effect, they were included; however, if they were associated with a subchronic or chronic effect, they were not captured in the database).

- A panel member expressed concern over the relatively small amount of effects data in EDPSD v.2. The member suggested that all of the QSAR and HPV data be incorporated into the database before Phase I. EPA stated that because of time constraints they would not be able to incorporate all of these data prior to Phase I, but will include them as they become available.

- One panel member suggested the incorporation of readily available effects data, such as data available from NTP and International Agency for Research on Cancer (IARC). Another panel member suggested incorporating the HPV initiative data into EDPSD v.2.

Data Source Quality

- One panel member commented that Registry of Toxic Effects of Chemical Substances (RTECS) is a superficial database and suggested Agency for Toxic Substances and Disease Registry (ATSDR) publications as better data sources for effects information.

- A panel member indicated concern about the effects studies presented in the Epidemiological and Clinical Data Compartment. The panel member suggested that many existing epidemiological and clinical studies may have been over-interpreted, and stated that some studies only present a hypothesis regarding the effects, whereas other studies show causal relationships. He indicated that EPA should focus its attention on the studies showing causal relationships. EPA stated that EDPSD v.2 is used for priority-setting and generation of the Tier 1 Screening List. EPA is not attempting to perform hazard assessments at this stage but raising a "red flag" for that chemical. Panel members then expressed concern that EPA may raise a "red flag" for the wrong chemical. EPA indicated that the chemical industry as well as the public will be given an opportunity to comment on EPA's priority list.

General Comments

- A panel member noted that effects data (especially neurotoxic effects) are simply not available for the HPV/pesticide other ingredients. EPA agreed and stated that the lack of such data is one reason for Tier 1 Screening.

7.6 Ranking Algorithms Used in the Human Effects Compartments

James Kwiat, US EPA, Office of Pollution Prevention and Toxics, Risk Assessment Division (OPPT/RAD)

Mr. Kwiat gave a brief introduction to the ranking algorithms used in the human effects compartments. His presentation can be viewed at *http://www.epa.gov/scipoly/oscpendo/prioritysetting/presentationsonthedatabase2.ppt*. During his presentation, he discussed the different ranking algorithms used for the effects data, and posed the following questions to the panel members:

- Do the ranking algorithms make sense?
- Do the panel members have any suggestions to improve or replace existing algorithms?

Panel members comments and EPA responses are summarized below.

- A panel member stated that he agreed with EPA's ranking approach.

- One panel member expressed concern over how the data should be handled when multiple studies present conflicting results for one chemical. The panel member suggested "throwing out" all of the data for a chemical when conflicting studies were found. A different panel member disagreed with this suggestion. EPA indicated that in the case of epidemiological/clinical data, the study with the highest relevance and quality rating is currently used for ranking purposes Additionally, other available studies are also presented in EDPSD v.2 for further analysis and review of a chemical. EPA stated that this method was used because of a fundamental need to condense the working data to address system functionality requirements.

- Several panel members expressed concern over the value judgements required when determining the Data Quality and Data Relevance ratings. EPA recognized that EDPSD v.2 is a dynamic system and that a number of judgement calls had to be made when evaluating data source ranking options. EPA stated that some level of value judgement was necessary for ranking these data sources.

- One panel member suggested that if multiple positive effect studies exist for a chemical then that chemical should have a higher ranking than chemicals with only one positive study. EPA indicated that they considered the benefits and drawbacks of a number of ranking methodologies for effects data. Based on the results of those discussions, the method currently used in the EDPSD v.2 was chosen.

- Panel members expressed concern over unclear documentation of data source priority. They would like the effects data source hierarchy presented in the User's Guide with the reasons why EPA selected the hierarchy.

7.7 Completeness and Quality of Data Sources and the Ranking Algorithms Used in the Ecological Effects Compartments

Dr. John Walker, US EPA, Office of Pollution Prevention and Toxics, Interagency Testing Committee (ITC)

Dr. Walker gave a presentation highlighting the methodologies used by EPA to assess and rank data in the ecological effects compartment. This presentation can be viewed at *http://www.epa.gov/scipoly/oscpendo/prioritysetting/presentationsonthedatabase2.ppt*. The main points of his presentation are summarized below.

- Potential sources of data for Ecotoxicity Compartment in EDPSD v.2 are:

  -- AQUIRE (already incorporated),
  -- Terrestrial Wildlife Toxicity Database (TERRETOX) (scheduled to be added),
  -- The Canada Herring Gull Databases (currently investigating), and
  -- Suggestions from the panel members.

- The process used to rank AQUIRE data is as follows:

  -- All species for which data were available were examined and representative species (warm and cold water fish, fresh and salt water fish, and invertebrates) were selected for incorporation into EDPSD v.2.
  -- The types of effects (reproductive, physiological, behavioral, and growth) summarized in AQUIRE were reviewed. EPA ranked the different types of effects equally. EPA also reviewed the endpoints provided in AQUIRE and ranked the effects from highest positive effect (MATC) to the lowest negative effect (NOAEL).
  -- AQUIRE data were reported using several types of concentration data. EPA selected the mean concentrations (Type 1) and maximum concentrations (Type 2), and weighted these concentration types equally for ranking purposes.

- Suggestions on how to improve the general quality of the ecological effects compartment are to:

  -- Separate organic and inorganic compounds,
  -- Organize the chemicals by mode of action (e.g., 4-nitro-phenol),

-- Use QSARs to predict effects, and
-- Collapse fish and invertebrate data to avoid artificially assigning a higher weight to a chemical.

Dr. Walker solicited comments from the panel on his presentation and on the following points:

- The proposed and actual ranking methods used by EPA,
- The species examined and EPA's rationale for selection,
- The effects preferences and endpoints used, and
- The concentration type units used.

The panel's comments on Dr. Walker's presentation and EPA's responses to these issues are summarized below.

Ecotoxicity Data Sources

- The panel expressed general concerns about the degree of coverage of ecological effects due to data availability and quality.

- Some panel members questioned why the TERRETOX data had not yet been incorporated. EPA stated that TERRETOX data in a format compatible with EDPSD v.2 were not available until May 25, 2000. EPA indicated that an effort was made to obtain a preliminary version, but one was not ready for release. EPA noted that if sufficient resources are available TERRETOX data will be imported into EDPSD v.2.

AQUIRE Data Editing

- Several panel members commented that the ecotoxicity compartment seemed truncated. The panel members stated that AQUIRE has numerous data points but by limiting the species included in EDPSD v.2, EPA excluded a large amount of data. Panel members recommended including additional species. EPA stated that they selected the most representative species; however, Dr. Walker indicated that EPA may include data associated with the Bluegill into EDPSD v.2.

- Some panel members also suggested relaxing the data quality codes used to extract data from AQUIRE. The panel members indicated that the screening process used by AQUIRE should be of high enough quality such that EPA does not have to further exclude data. One panel member noted that AQUIRE was populated based on a data search of aquatic literature and international data sources. Some panel member indicated that these toxicological studies are representative of studies being performed around the world. He also indicated that AQUIRE captures field studies, peer reviewed studies, and gray literature, and that AQUIRE data should be

considered of high quality. The panel members indicated that a more complete data set is preferred; however; other panel members agreed with EPA's proposed data quality criteria.

- Panel members questioned whether both HPV/ pesticide other ingredients and PAIs were included in the Ecotoxicity Effects Compartment. EPA indicated that the compartment contains data for 37 HPV/pesticide other ingredients and 271 additional chemicals. Some of the 271 chemicals are PAIs. The panel suggested that EPA should indicate which of these chemicals are PAIs.

- Panel members were concerned over the lack of data for invertebrates.

Public Comments

- A public commenter suggested investigating the ecological effects of pharmaceuticals. The commenter urged EPA to consider adding pharmaceuticals to EDPSD v.2. A panel member also suggested investigating the effects of pharmaceuticals that were designed to be endocrine disruptors (e.g., birth control pills) and are released into the environment. EPA indicated that although the focus of Phase I is HPV/pesticide other ingredients, it does not mean that EPA will not investigate other categories; however, pharmaceuticals are regulated by FDA. EPA stated that because pharmaceuticals have been extensively reviewed, Tier 1 screening should not be necessary, these chemicals are expected to proceed directly to Hazard Assessment. EPA also noted that the QSARs evaluated will also include pharmaceuticals that may be structurally related to the HPV/pesticide other ingredients.

Ranking Algorithms

- One panel member stated that he agreed with the method EPA used when weighting effects (all effects were weighted equally).

7.8 Definition and Ranking Procedure of the Combined Compartments

James Kwiat, US EPA, Office of Pollution Prevention and Toxics, Risk Assessment Division (OPPT/RAD)

Mr. Kwiat presented background information on the combination of exposure- and effects- related information into one category. His presentation can be viewed at *http://www.epa.gov/scipoly/oscpendo/prioritysetting/presentationsonthedatabase2.ppt*. The key points of his presentation are summarized below.

- The Combined Exposure- and Effects-Related Information Category consists of four compartments, two of which are related to human effects and exposures and two of which are related to ecological effects and exposures.

- The current process of combining the effects and exposure data is not an actual risk assessment or data interpretation; it is simply a combination of ranks. For example, in the Combined Human Biomonitoring and Effects Data Compartment, the ranking was based on the average of the t rank in the Human Biological Monitoring Data Compartment and the highest rank in any human health effects compartment.

Mr. Kwiat posed the following questions related to the combined compartments and then solicited comments from the panel members.

- Does the ranking approach make sense?

- Do the panel members have any suggestions to improve or replace the existing approach?

The panel members comments and EPA responses are summarized below.

- Panel members indicated that the use of QSARs will allow the most flexibility in use of the combined compartment. For example, a QSAR for DES can be used to predict the effects related to other chemicals with similar structures. QSARs will also be useful for cases where a large amount of exposure data exists for a particular chemical with no associated effects data, but QSAR data is available for a chemical with a similar structure.

- A panel member recommended incorporating water quality data (Total Maximum Daily Loads or TMDLs) into the ranking scenarios. The panel member thought water quality data are a good indicator of the level at which chemicals are present in a water source. The water quality data could be used with the Surface Water Monitoring Data Exposure Compartment in the Combined Exposure and Effects-Related Information Category.

- Panel members suggested EPA proceed cautiously when combining data sources in the Combined Exposure- and Effects-Related Information Category, and to verify that the data groupings “make sense”.

- Panel members commented that the original intent of the combined category (as defined by the EDSTAC committee) was to capture chemicals that would not be selected based on exposure or effects data alone because they were not high hazard or high exposure chemicals. The chemicals

selected in the combined category were intended to represent chemicals with a moderate level of risk and a moderate level of exposure.

- Several panel members suggested converting the combined effects and exposure ranks to "scores". Instead of calculating an average rank based on a combination of these two ranks, EPA should calculate a score by multiplying the effects score and the exposure score. This method would allow EPA to identify chemicals found in the environment at moderate levels and that pose a moderate risk.

- A panel member wondered whether, if Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) changes are made to the inert categories for the PAIs, would those chemicals automatically be removed from EDPSD v.2. EPA indicated that currently the 4A chemicals are flagged as exempt, and that all of the PAIs are being analyzed.

- Some panel members expressed concern over how the PAIs would be incorporated into EDPSD v.2. EPA stated that the PAIs would not be incorporated into EDPSD v.2 but reviewed simultaneously with the priority list generated by EDPSD v.2. EPA also indicated that it is expected that many of the PAIs will go directly to Tier 2 Testing or Hazard Assessment and will not be assessed using Tier 1 Screening.

- Panel members questioned how the PAI data would be used in the combined compartments.

- A panel member stated that the combined category structure proposed by EPA made sense.

7.9 Database Default Weights

James Darr, US EPA, Office of Pollution Prevention and Toxics, Exposure Assessment Branch (OPPT/EAB)

Mr. Darr gave a brief overview of the database default weights. His presentation can be viewed at *http://www.epa.gov/scipoly/oscpendo/prioritysetting/presentationsonthedatabase2.ppt*. The main principles used to develop the default weights are presented below.

- The combined category was assigned a greater weight than either the effects or exposure categories;

- Slightly higher weight was assigned to the effects category than to the exposure category;

- In the combined exposure and effects category, a higher weight was assigned to the compartment for which more definitive exposure data exist;

- Equal weight was assigned to each of the exposure compartments;

- The Epidemiological and Clinical, Reproductive/Developmental Toxicity, Chronic/Subchronic Toxicity, and Carcinogenicity Compartments were assigned equal weights; and

- The overall human health compartments were assigned weights equal to the Ecotoxicity Compartment.

The panel member comments on the default weights used by EDPSD v.2 are presented below:

- Panel members expressed concern over potential compartment double counting as a result of the weightings in both the Exposure or Effects Category and the Combined Exposure- and Effects-Related Information Category. EPA stated that some chemicals will be selected based on their rank in the exposure category, some will selected based on their rank in the effects category, and other chemicals will be selected based on their rank in the combined category. This methodology was agreed upon by the EDSTAC committee.

- One panel member suggested developing a summary table that presents all of the data sources and compartments and their associated weights (including weights of zero). The panel member also suggested adding this discussion to the text of the User's Guide.

<u>Exposure Compartments</u>

- Some panel members were concerned that all compartments in the exposure category were assigned the same weight.

- One panel member thought that the Human Biological Monitoring Data Compartment should have a higher weight than the Chemicals in Consumer/Cosmetic Products Compartment because the data sources under the Human Biological Monitoring Data Compartment are actual measurements of exposure. EPA stated that a higher weight was associated with the Human Biological Monitoring Data Compartment because of the Combined Exposure- and Effects-Related Information Category.

- One panel member had expected that Toxic Release Inventory (TRI) data would have been assigned a higher weight. This expectation was based on the concept that TRI provides the best analysis of exposure because it is a

compilation of all reported releases of all TRI chemicals, regardless of their effects.

- A panel member recommended that the Occupational Exposure Chemicals Compartment be assigned a weight of zero. The member stated that most people are not exposed to chemicals at the TLV, PEL, and REL levels and therefore these data sources are not appropriate for measuring occupational exposure.

Effects Compartments

- One panel member expressed concern over the 25% weight assigned to the effects category. He indicated that if the most complete set of chemicals possible was not used in the database, then EPA should downplay the priority given to this category. He stated that a chemical may not show up in the data sources if it were not tested, rather than because no effect is noted.

- One panel member noted that the 13% weight allocated for the Ecotoxicity Compartment seemed high, especially if the compartment did not contain terrestrial, amphibian, and avian species. EPA commented that they intend to include these species in EDPSD v.2 through the inclusion of TERRETOX and other data sources.

- Some panel members expressed concern over the human biomonitoring effects data. A panel member stated that the data represented are limited, and only few chemicals were represented (the same chemicals that are typically scanned for as part of the adipose tissue screens). Some of the panel members did not agree that these chemicals should be given a higher priority because they were detected in human tissue. One panel member stated that these data place a bias on chemicals with known effects because these chemicals are the ones that are screened for during testing. Other panel members strongly disagreed with these comments and stated that human biomonitoring data represent the best available measurement of exposure.

Combined Category

- Some of the panel members indicated the weight associated with the combined category was too high. Other panel members suggested increasing the weight associated with the Combined Exposure- and Effects-Information Category.

General Comments

- Panel members expressed concerns that the "data rich" chemicals are more likely to be selected because of the weighting factors assigned by EPA.

- A panel member suggested that if a compartment has a large amount of data, that compartment should receive a higher weight than a compartment with less data.

7.10 Panel Discussion of Decision to Focus on HPV/ Pesticide Other Ingredients and PAIs

- Panel members were concerned over the resolution of EDPSD v.2 if its focus is primarily the intersection of HPV chemicals and pesticide other ingredients. EPA indicated that approximately 600 chemicals are in the current database of HPV/pesticide other ingredients overlaps. The Tier 1 Screening List will contain HPV chemicals, pesticide other ingredients , and PAIs.

- Panel members asked EPA how the Tier 1 Screening List would be broken out among the three types of chemicals (HPV, pesticide other ingredients, and PAIs). EPA indicated this information is not available at this time, but that the screening stage would play a key role in the development of the final list.

- After much discussion and some reservations, the panel members agreed with EPA's policy decision to focus on HPV, pesticide other ingredients and PAIs. The panel members want to confirm that the nominations compartment could be used for non-HPV/pesticide other ingredients. EPA indicated that these types of nominations would be accepted.

7.11 Other Questions Related to EDPSD v.2 Posed by EPA to the Panel

At the beginning of Day Three, EPA posed the following questions to the panel members:

- How should out-of-production chemicals be handled (e.g., ozone depleting chemicals)?

- Do any of the panel members have comments on EPA's method of sorting? EPA changed where/when sorting occurs - it now occurs after the initial priority setting.

The panel's suggestions and comments are presented below.

Out-of-Production Chemicals

- Panel members suggested that the chemicals should be closer to actual phase out prior to removing them from the database because of issues such as persistence and resistance to biodegradation.

- One panel member suggested a case by case analysis of the out-of-production or phased out chemicals. He also suggested including the PAIs even if they are phased out because they may still be used for agricultural purposes, and may remain in the environment.

- A panel member noted that 1,1,1-Trichloroethane has been phased out of production and is no longer on the list of pesticide other ingredients (as are CFCs) but still appears in EPA's database. The panel member recommended removing this chemical from the database.

Sorting

- The panel members agreed with EPA's sorting approach.

Other topics of discussion and the comments from the panel members are presented below.

Second Pass Chemical Selection Approach

- Panel members discussed the chemical selection process used in EDPSD v.2 for the "Second Pass." Currently during the first pass, the system selects chemicals from each compartment based on the assigned weights. If after the first pass, the target number of chemicals has not been reached, the system performs a second pass. During the second pass, EDPSD v.2 selects one chemical from each compartment, regardless of the assigned weight. The panel members had several comments on the current method and suggested alternative approaches.

  -- Several panel members suggested stopping the chemical selection process after the first pass. If the target number of chemicals was not reached, the user could incrementally increase the target number of chemicals until the number of chemicals they wanted was obtained.
  -- Some panel members suggested allowing the user to stop the selection process after the first pass was completed, and then run the second pass after the user had a chance to evaluate the first pass Tier 1 Screening List.

  -- Panel members also suggested that EDPSD v.2 select additional chemicals on the second pass from the most heavily weighted

compartments until it reaches the target number of chemicals, rather than selecting one additional chemical from all of the compartments.

Mixtures

- A panel member asked EPA why the mixtures compartment currently has a weight of zero. EPA indicated that the SAB recommend that they hold off on incorporating mixtures into EDPSD v.2 until the single chemical approach was complete. EPA reiterated that the current policy decision was to focus on HPV/pesticide other ingredients, but that mixtures would be considered in the future. Several panel members suggested adding mixtures at this point. A panel member suggested incorporating at least one mixture, possibly one of the mixtures recommended by EDSTAC, into the Nominations Compartment of EDPSD v.2. EPA stated that they were approaching Mixtures as a research project and that the project had just received funding.

General Comments

- One panel member was concerned over when animal testing would occur. EPA indicated that testing would not be started until database is "complete" for Phase I and that preliminary QSARs will be incorporated during this phase. EPA indicated that the database will never be fully "complete" as it designed so that data can always be added and updated. EPA also stated that Phase II will incorporate the results of Phase I.

- A panel member suggested that EPA rank chemicals based on the criteria presented and incorporate a production level cut-off.

- One panel member questioned why the Naturally Occurring Non-Steroidal Estrogens Compartment was assigned a weight of zero. EPA indicated that EDPSD v.2 is a work in progress, and that this compartment is under development. The panel member stated that this zero weight creates an unbalanced view and asked if NONEs could be nominated. EPA indicated that these chemicals could be nominated.

8.0 PUBLIC COMMENTS ON WORKSHOP DAY 2 AND DAY 3

Public Attendees; **EPA Representatives**

At the end of the workshop, the floor was opened to public commenters. A list of public attendees is included as Appendix C. A summary of the public comments is presented below.

- One commenter stated that although EPA has made progress, more work still needs to be completed, including the integration of the HPV Challenge Data. He indicated that the data quality issues were well covered during the workshop. The main points of his comment are presented below:

  -- He does not want EPA to relax its data quality standards for Phase I.
  -- He recommended validating the QSARs prior to incorporating them into EDPSD v.2.
  -- He indicated that the combined category approach was appropriate.
  -- He noted that a large number of chemicals exist in the environment that EPA should include in their analysis. He agreed with the policy decision to focus on HPV/pesticide other ingredients and PAIs but wanted EPA to indicate to the public that these chemicals are not the only chemicals of concern.

- A commenter stated that although this workshop was his first time seeing the approach developed by EPA, he indicated that it is a step in the right direction, and that he appreciates being allowed to comment at the beginning of the process.

- One commenter expressed concern over how EDPSD v.2 was developed. A summary of his comments is presented below.

  -- He indicated that EPA excluded scientific voices during the development of EDPSD v.2.
  -- He stated that the compartment-based approach is irrational and a good alternative to this approach is a risk-based approach. He stated that the risk-based approach is a much easier model and queried why EPA had not used this approach.
  -- He implied that the EDSTAC Committee was controlled by stakeholders favoring the EPA's position and that EPA held several closed workshops. Although the scientific community wanted to be involved they were not.
  -- He indicated that priority setting is crucial and necessary. He stated that he has done studies on NTP Nominations, he has found that production of chemicals drops when they are nominated, not after being studied and the results from the studies are published

Mr. Timm of EPA responded to these comments. His response is presented below.

- EPA indicated that the EDSTAC committee was not comprised of only EPA employees. EPA stated that EPA held a public meeting announcing EDSTAC in May 1996. Facilitators helped select a workable number of stakeholders for the EDSTAC Committee. They gave consideration to all stakeholders; industry, academia, government entities, and non-government entities were included in the EDSTAC Committee. EPA indicated that a free debate on all components of the final system took place and that real differences of opinion existed across the committee.

- EPA stated that a risk-based system is a good idea but due to the limited amount of effects data, a risk-based analysis cannot be performed for most chemicals. The current compartment-based approach can be used to complete analyses even if effects data do not exist.

9.0 NEXT STEPS

Patrick Kennedy, US EPA, Office of Pollution Prevention and Toxics, Exposure Assessment Branch (OPPT/EAB)

Mr. Kennedy stated that a summary of this workshop will be posted on *http://www.epa.gov/scipoly/oscpendo/prioritysetting/presentationsonthedatabase2.ppt* by July 21, 2000. The panel members and the public will have 30 days to comment on the summary.

EPA will address many of the issues raised during the workshop including:

- Incorporating additional data sources;
- Incorporating comments raised during the workshop; and
- Performing "What-If" exercises.

Mr. Kennedy reviewed the schedule for generating the Tier 1 Screening List.

- He indicated one of the time-limiting steps will be the availability of the QSARs. He stated that EPA will not release an updated version of EDPSD v.2 before the QSARs are incorporated.

- Once the QSARs are incorporated, EDPSD v.2 will go through an external peer review.

- The next step will be to generate a draft Tier 1 Screening List for internal review. The draft Tier 1 Screening list will be generated for public comment by the end of 2001. By 2003 the test batteries should be developed, and validated. Panel members indicated EPA should keep the time relatively short between when the list is released to the public and when screening occurs.

APPENDIX A
Public Workshop Agenda

AGENDA

Monday, June 5 Overview of the Endocrine Disruptor Screening Program

- Welcome
- Overview of the Endocrine Disruptor Screening Program
- Standardization and Validation Activities
- Questions
- OPP Activities to Prioritize Pesticide Active Ingredients
- Questions on Prioritization of Active Ingredients
- Lunch
- Public Comments on the Endocrine Disruptor Screening Program, Standardization/Validation Activities, or the OPPActives Approach
- Break
- Demo of EDPSD Version 2
- End of Demo

Tuesday, June 6 Panel Discussion of the Priority Setting Database (Exposure & Effects)

- Overview of the Current Status of the EDPSD
- Completeness and Quality of Data Sources Used in Exposure Compartments
- Break
- Ranking Algorithms Used in Exposure Compartments
- Completeness and Quality of Data Sources Used in Human Effects Compartments
- Lunch
- Ranking Algorithms Used in Human Effects Compartments
- Break
- Completeness and Quality of Data Sources Used in Ecological Effects Compartments
- Ranking Algorithms Used in Ecological Effects Compartments
- Public Comments on Ecological Effects in EDPSD
- Definition and Ranking Procedure of the Combined Compartments
- End of day

Wednesday, June 7 Panel Discussion of the Priority Setting Database (Exposure and Effects and Weights)

- Additional Discussion of Exposure and Effects Compartments
- Break
- Discussion of Database Default Weights and Ranked List of HPV/ Pesticide Other Ingredients
- Discussion of “What-If” Scenarios
- Public Comments on EDPSD
- End of Workshop

APPENDIX B
Invited Participants

INVITED PARTICIPANTS TO JUNE 2000 ENDOCRINE DISRUPTOR PRIORITY-SETTING WORKSHOP

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APPENDIX C
Workshop Sign-in Sheet

ENDOCRINE WORKSHOP SIGN-IN SHEET

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